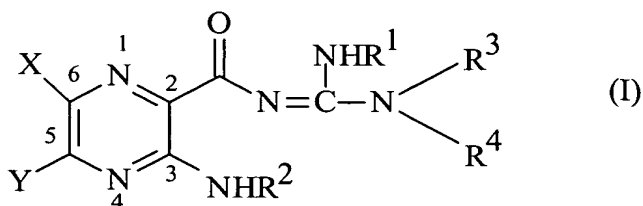


IN THE CLAIMS

The status of each claim is presented below.

1. (Twice Amended) A compound represented by formula (I):



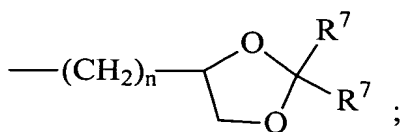
wherein

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

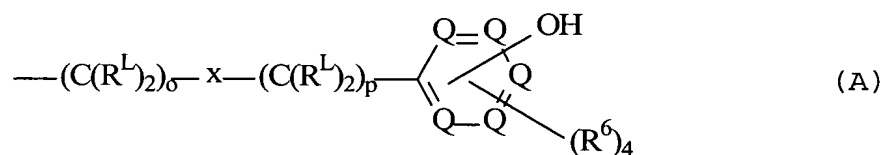
Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or $-N(R^2)_2$;

R^1 is hydrogen or lower alkyl;

each R^2 is, independently, $-R^7$, $-(CH_2)_m-OR^8$, $-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$, $-(CH_2)_n-Z_g-R^7$, $-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2)_n-CO_2R^7$, or

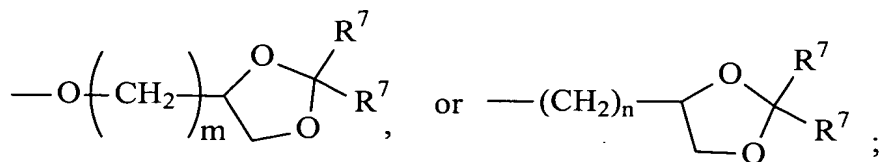


R^3 and R^4 are each, independently, hydrogen, a group represented by formula (A), lower alkyl, hydroxy lower alkyl, phenyl, phenyl-lower alkyl, (halophenyl)-lower alkyl, lower-(alkylphenylalkyl), lower alkoxyphenyl)-lower alkyl, naphthyl-lower alkyl, or pyridyl-lower alkyl, with the proviso that at least one of R^3 and R^4 is a group represented by formula (A):



wherein

each R^{L} is, independently, $-\text{R}^7$, $-(\text{CH}_2)_n-\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{OR}^8$, $-(\text{CH}_2)_n-\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-(\text{Z})_g-\text{R}^7$, $-\text{O}-(\text{CH}_2)_m-(\text{Z})_g-\text{R}^7$, $-(\text{CH}_2)_n-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-(\text{CH}_2)_n-\text{CO}_2\text{R}^7$, $-\text{O}-(\text{CH}_2)_m-\text{CO}_2\text{R}^7$, $-\text{OSO}_3\text{H}$, $-\text{O-glucuronide}$, $-\text{O-glucose}$, or



each x is, independently, O, NR⁷, C=O, CHOH, C=N-R⁶, or represents

a single bond;

each o is, independently, an integer from 0 to 10;

each p is, independently, an integer from 0 to 10;

with the proviso that (a) the sum of o and p in each contiguous chain is

from 1 to 10 when x is O, NR⁷, C=O, or C=N-R⁶ or (b) that the sum of o and p

in each contiguous chain is from 5 to 10 ~~4 to 10~~ when x represents a single bond;

each R⁶ is, independently, -R⁷, -OH, -OR¹¹, -N(R⁷)₂, -(CH₂)_m-OR⁸,

-O-(CH₂)_m-OR⁸, -(CH₂)_n-NR⁷R¹⁰, -O-(CH₂)_m-NR⁷R¹⁰,

-(CH₂)_n(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -O-(CH₂)_m(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,

-(CH₂CH₂O)_m-R⁸, -O-(CH₂CH₂O)_m-R⁸, -(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰,

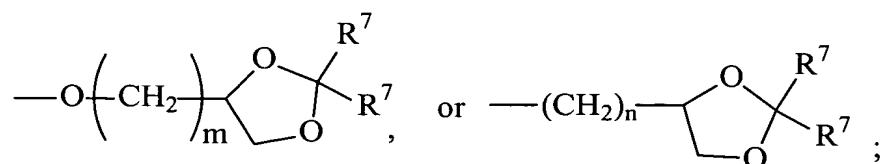
-O-(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰, -(CH₂)_n-C(=O)NR⁷R¹⁰,

-O-(CH₂)_m-C(=O)NR⁷R¹⁰, -(CH₂)_n-(Z)_g-R⁷, -O-(CH₂)_m-(Z)_g-R⁷,

-(CH₂)_n-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,

-O-(CH₂)_m-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,

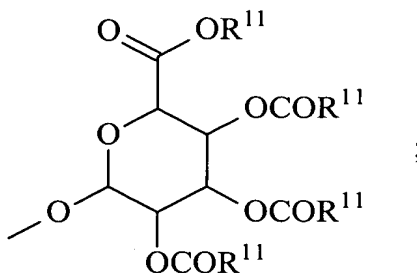
-(CH₂)_n-CO₂R⁷, -O-(CH₂)_m-CO₂R⁷, -OSO₃H, -O-glucuronide, -O-glucose,



wherein when two R⁶ are -OR¹¹ and are located adjacent to each other on a phenyl ring, the alkyl moieties of the two R⁶ may be bonded together to form a methylenedioxy group;

each R^7 is, independently, hydrogen or lower alkyl;

each R^8 is, independently, hydrogen, lower alkyl, $-C(=O)-R^{11}$, glucuronide, 2-tetrahydropyranyl, or



each R^9 is, independently, $-\text{CO}_2R^7$, $-\text{CON}(R^7)_2$, $-\text{SO}_2\text{CH}_3$, or $-C(=O)R^7$;

each R^{10} is, independently, $-\text{H}$, $-\text{SO}_2\text{CH}_3$, $-\text{CO}_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, or $-\text{CH}_2-(\text{CHOH})_n-\text{CH}_2\text{OH}$;

each Z is, independently, CHOH , $\text{C}(=\text{O})$, CHNR^7R^{10} , $\text{C}=\text{NR}^{10}$, or NR^{10} ;

each R^{11} is, independently, lower alkyl;

each g is, independently, an integer from 1 to 6;

each m is, independently, an integer from 1 to 7;

each n is, independently, an integer from 0 to 7;

each Q is, independently, $\text{C}-R^6$;

or a pharmaceutically acceptable salt thereof, and

inclusive of all enantiomers, diastereomers, and racemic mixtures thereof.

2. (Previously Presented) The compound of Claim 1, wherein Y is $-\text{NH}_2$.

3. (Previously Presented) The compound of Claim 2, wherein R^2 is hydrogen.
4. (Previously Presented) The compound of Claim 3, wherein R^1 is hydrogen.
5. (Previously Presented) The compound of Claim 4, wherein X is chlorine.
6. (Previously Presented) The compound of Claim 5, wherein R^3 is hydrogen.
7. (Previously Presented) The compound of Claim 6, wherein each R^1 is hydrogen.
8. (Previously Presented) The compound of Claim 7, wherein o is 4.
9. (Previously Presented) The compound of Claim 8, wherein p is 0.
10. (Previously Presented) The compound of Claim 9, wherein x represents a single bond.
11. (Previously Presented) The compound of Claim 10, wherein each R^6 is hydrogen.
12. Canceled.
13. Canceled.

14. (Previously Presented) The compound of Claim 1, wherein

X is halogen;

Y is $-N(R^7)_2$;

R^1 is hydrogen or C_1 - C_3 alkyl; and

R^2 is $-R^7$, $-(CH_2)_m-OR^7$, or $-(CH_2)_n-CO_2R^7$;

R^3 is a group represented by formula (A); and

R^4 is hydrogen, a group represented by formula (A), or lower alkyl.

15. (Previously Presented) The compound of Claim 14, wherein

X is chloro or bromo;

Y is $-N(R^7)_2$;

R^2 is hydrogen or C_1 - C_3 alkyl;

at most three R^6 are other than hydrogen as defined above; and

at most three R^L are other than hydrogen as defined above.

16. (Previously Presented) The compound of Claim 15, wherein Y is $-NH_2$.

17. (Previously Presented) The compound of Claim 16, wherein

R^4 is hydrogen;

at most one R^L is other than hydrogen as defined above; and

at most two R^6 are other than hydrogen as defined above.

18. (Previously Presented) The compound of Claim 17, wherein x is O, NR⁷, C=O, CHOH, or C=N-R⁶.
19. (Previously Presented) The compound of Claim 17, wherein x represents a single bond.
20. (Previously Presented) The compound of Claim 1, wherein x is O, NR⁷, C=O, CHOH, or C=N-R⁶.
21. (Previously Presented) The compound of Claim 1, wherein x represents a single bond.
22. (Previously Presented) The compound of Claim 1, wherein each R⁶ is hydrogen.
23. (Previously Presented) The compound of Claim 1, wherein at most two R⁶ are other than hydrogen as defined in Claim 1.
24. (Previously Presented) The compound of Claim 1, wherein one R⁶ is other than hydrogen as defined in Claim 1.
25. (Previously Presented) The compound of Claim 1, wherein one R⁶ is -OH.
26. (Previously Presented) The compound of Claim 1, wherein each R^L is hydrogen.

27. (Previously Presented) The compound of Claim 1, wherein at most two R^L are other than hydrogen as defined in Claim 1.

28. (Previously Presented) The compound of Claim 1, wherein one R^L is other than hydrogen as defined in Claim 1.

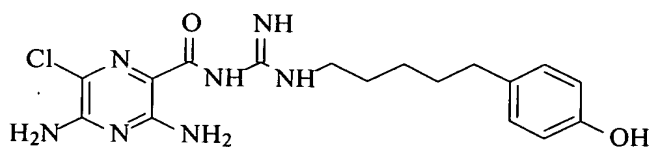
29. (Currently Amended) The compound of Claim 1, wherein x represents a single bond and the sum of o and p is 4 to 6.

30. Canceled.

31. Canceled.

32. (Currently Amended) The compound of Claim 1 ~~31~~, which is in the form of a hydrochloride salt.

33. (Previously Presented) The compound of Claim 1, which is represented by the formula

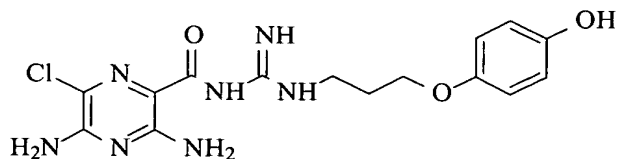


34. (Previously Presented) The compound of Claim 33, which is in the form of a pharmaceutically acceptable salt.

35. (Previously Presented) The compound of Claim 34, which is in the form of a hydrochloride salt.

36-41. Canceled.

42. (Previously Presented) The compound of Claim 1, which is represented by the formula



43. (Previously Presented) The compound of Claim 42, which is in the form of a pharmaceutically acceptable salt.

44. (Previously Presented) The compound of Claim 43, which is in the form of a hydrochloride salt.

Application No.:10/076,551

In reply to Office Action of September 12, 2003

45-47. Canceled.

48. (Previously Presented) The compound of Claim 1, which is in the form of a pharmaceutically acceptable salt.

49. (Previously Presented) A pharmaceutical composition, comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

50. Canceled.

51. (Canceled).

52. (Previously Presented) A method of blocking sodium channels, comprising: contacting sodium channels with an effective amount of the compound of Claim 1.

53-79. (Canceled).

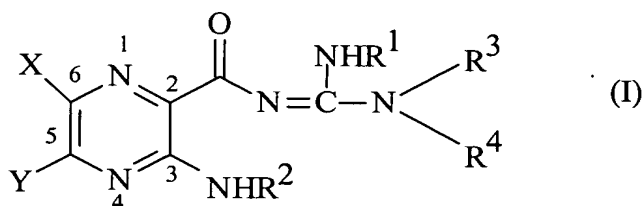
80. (Previously Presented) A composition, comprising:
the compound of Claim 1; and
a P2Y2 inhibitor.

81. (Previously Presented) A composition, comprising:
the compound of Claim 1; and

a bronchodilator.

82. (New) The compound of Claim 1, which is in the form of a mesylate salt.

83. (New) A compound represented by formula (I):



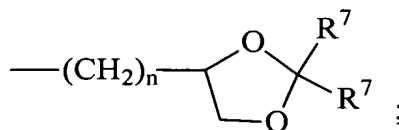
wherein

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

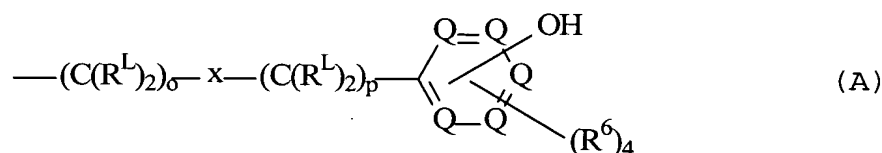
Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or -N(R²)₂;

R¹ is hydrogen or lower alkyl;

each R² is, independently, -R⁷, -(CH₂)_m-OR⁸, -(CH₂)_m-NR⁷R¹⁰, -(CH₂)_n(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -(CH₂CH₂O)_m-R⁸, -(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰, -(CH₂)_n-C(=O)NR⁷R¹⁰, -(CH₂)_n-Z_g-R⁷, -(CH₂)_m-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -(CH₂)_n-CO₂R⁷, or



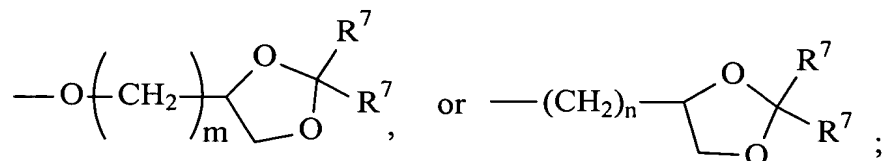
R^3 and R^4 are each, independently, hydrogen, a group represented by formula (A), lower alkyl, hydroxy lower alkyl, phenyl, phenyl-lower alkyl, (halophenyl)-lower alkyl, lower-(alkylphenylalkyl), lower alkoxyphenyl)-lower alkyl, naphthyl-lower alkyl, or pyridyl-lower alkyl, with the proviso that at least one of R^3 and R^4 is a group represented by formula (A):



wherein

each R^L is, independently, $-\text{R}^7$, $-(\text{CH}_2)_n-\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{OR}^8$, $-(\text{CH}_2)_n-\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-(\text{Z})_g-\text{R}^7$, $-\text{O}-(\text{CH}_2)_m-(\text{Z})_g-\text{R}^7$, $-(\text{CH}_2)_n-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$,

$-(\text{CH}_2)_n-\text{CO}_2\text{R}^7$, $-\text{O}-(\text{CH}_2)_m-\text{CO}_2\text{R}^7$, $-\text{OSO}_3\text{H}$, $-\text{O}$ -glucuronide, $-\text{O}$ -glucose, or



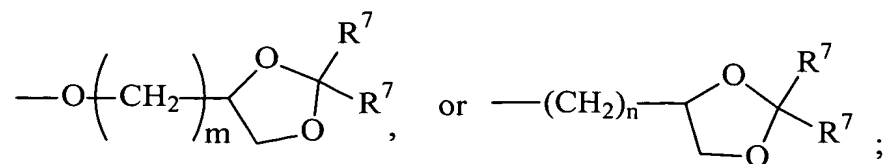
each x is, independently, O, NR^7 , $\text{C}=\text{O}$, CHOH , $\text{C}=\text{N}-\text{R}^6$, or represents a single bond;

each o is, independently, an integer from 0 to 10;

each p is, independently, an integer from 0 to 10;

with the proviso that (a) the sum of o and p in each contiguous chain is from 1 to 10 when x is O, NR^7 , $\text{C}=\text{O}$, or $\text{C}=\text{N}-\text{R}^6$ or (b) that the sum of o and p in each contiguous chain is from 4 to 10 when x represents a single bond;

each R^6 is, independently, $-\text{R}^7$, $-\text{OH}$, $-\text{OR}^{11}$, $-\text{N}(\text{R}^7)_2$, $-(\text{CH}_2)_m-\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{OR}^8$, $-(\text{CH}_2)_n-\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-(\text{Z})_g-\text{R}^7$, $-\text{O}-(\text{CH}_2)_m-(\text{Z})_g-\text{R}^7$, $-(\text{CH}_2)_n-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-(\text{CH}_2)_n-\text{CO}_2\text{R}^7$, $-\text{O}-(\text{CH}_2)_m-\text{CO}_2\text{R}^7$, $-\text{OSO}_3\text{H}$, $-\text{O}$ -glucuronide, $-\text{O}$ -glucose,

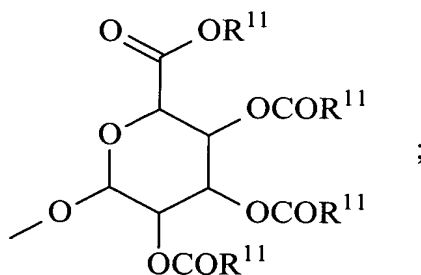


wherein when two R^6 are $-OR^{11}$ and are located adjacent to each other on a phenyl ring, the alkyl moieties of the two R^6 may be bonded together to form a methylenedioxy group;

with the proviso that at least one R^6 is other than hydrogen as defined above;

each R^7 is, independently, hydrogen or lower alkyl;

each R^8 is, independently, hydrogen, lower alkyl, $-C(=O)-R^{11}$, glucuronide, 2-tetrahydropyranyl, or



each R^9 is, independently, $-CO_2R^7$, $-CON(R^7)_2$, $-SO_2CH_3$, or $-C(=O)R^7$;

each R^{10} is, independently, $-H$, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$,

$-C(=O)R^7$, or $-CH_2-(CHOH)_n-CH_2OH$;

each Z is, independently, $CHOH$, $C(=O)$, $CHNR^7R^{10}$, $C=NR^{10}$, or NR^{10} ;

each R^{11} is, independently, lower alkyl;

each g is, independently, an integer from 1 to 6;

each m is, independently, an integer from 1 to 7;

each n is, independently, an integer from 0 to 7;

each Q is, independently, $C-R^6$;

or a pharmaceutically acceptable salt thereof, and

inclusive of all enantiomers, diastereomers, and racemic mixtures thereof.

84. (New) The compound of Claim 83, wherein Y is $-NH_2$.

85 (New) The compound of Claim 84, wherein R^2 is hydrogen.

86. (New) The compound of Claim 85, wherein R^1 is hydrogen.

87. (New) The compound of Claim 86, wherein X is chlorine.

88. (New) The compound of Claim 87, wherein R^3 is hydrogen.

89. (New) The compound of Claim 88, wherein each R^L is hydrogen.

90. (New) The compound of Claim 89, wherein o is 4.

91. (New) The compound of Claim 90, wherein p is 0.

92. (New) The compound of Claim 91, wherein x represents a single bond.

93. (New) The compound of Claim 83, wherein
 X is halogen;

Y is $-N(R^7)_2$;

R^1 is hydrogen or C_1-C_3 alkyl; and

R^2 is $-R^7$, $-(CH_2)_m-OR^7$, or $-(CH_2)_n-CO_2R^7$;

R^3 is a group represented by formula (A); and

R^4 is hydrogen, a group represented by formula (A), or lower alkyl.

94. (New) The compound of Claim 93, wherein

X is chloro or bromo;

Y is $-N(R^7)_2$;

R^2 is hydrogen or C_1-C_3 alkyl;

at most three R^6 are other than hydrogen as defined above; and

at most three R^L are other than hydrogen as defined above.

95. (New) The compound of Claim 94, wherein Y is $-NH_2$.

96. (New) The compound of Claim 95, wherein

R^4 is hydrogen;

at most one R^L is other than hydrogen as defined above; and

at most two R^6 are other than hydrogen as defined above.

97. (New) The compound of Claim 96, wherein x is O, NR^7 , $C=O$, $CHOH$, or $C=N-R^6$.

98. (New) The compound of Claim 96, wherein x represents a single bond.

99. (New) The compound of Claim 83, wherein x is O, NR^7 , $C=O$, $CHOH$, or $C=N-R^6$.

100. (New) The compound of Claim 83, wherein x represents a single bond.

101. (New) The compound of Claim 83, wherein at most two R^6 are other than hydrogen as defined in Claim 1.

102. (New) The compound of Claim 83, wherein one R^6 is -OH.

103. (New) The compound of Claim 83, wherein each R^L is hydrogen.

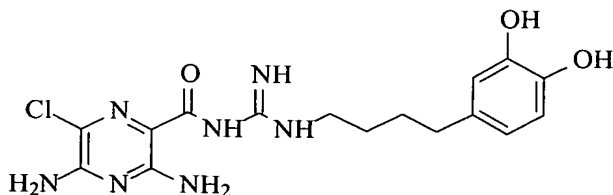
104. (New) The compound of Claim 83, wherein at most two R^L are other than hydrogen as defined in Claim 83.

105. (New) The compound of Claim 83, wherein one R^L is other than hydrogen as defined in Claim 83.

106. (New) The compound of Claim 83, wherein x represents a single bond and the sum of o and p is 4 to 6.

107. (New) The compound of Claim 83, which is in the form of a hydrochloride salt.

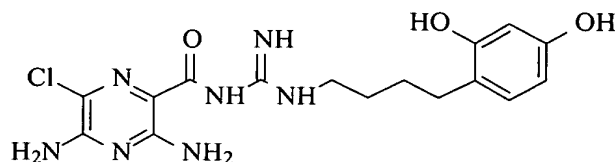
108. (New) The compound of Claim 83, which is represented by the formula



109. (New) The compound of Claim 108, which is in the form of a pharmaceutically acceptable salt.

110. (New) The compound of Claim 109, which is in the form of a hydrochloride salt.

111. (New) The compound of Claim 83, which is represented by the formula



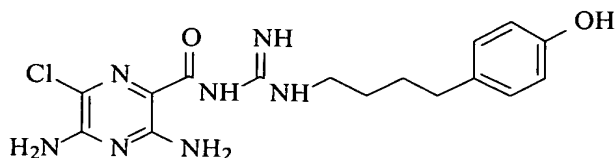
112. (New) The compound of Claim 111, which is in the form of a pharmaceutically acceptable salt.

113. (New) The compound of Claim 112, which is in the form of a hydrochloride salt.

114. (New) The compound of Claim 83, which is in the form of a pharmaceutically acceptable salt.

115. (New) A pharmaceutical composition, comprising the compound of Claim 83 and a pharmaceutically acceptable carrier.

116. (New) A compound represented by the formula



in the form of a pharmaceutically acceptable salt.

117. (New) The compound of Claim 116, which is in the form of a hydrochloride salt.

118. (New) The compound of Claim 116, which is in the form of a mesylate salt.

119. (New) A method of blocking sodium channels, comprising:
contacting sodium channels with an effective amount of the compound of any one of Claims 2-11, 14-29, 32-35, 42-44, 48, and 82-118.

120. (New) A method of blocking sodium channels, comprising:
contacting sodium channels with an effective amount of the composition of any one of Claims 49, 80, and 81.